

the chemotherapeutic compound having the capability of

- exerting a cytotoxic action toward actively proliferating cells,
- not affecting survival and proliferative potential of interphase cells,

the protective compound having the capability of

- reversibly inhibiting cytodieresis of normal cells,
- not inhibiting the biological action of said chemotherapeutic compound and,

wherein a pre-treatment with said protective compound is carried out before the combined treatment with class A and class B compounds and the administration of said protective compound results in the protection of at least part of said proliferating normal cells.

29. (new) The method according to claim 28, wherein the pre-treatment with the protective compound results in the arrest at interphase of at least part of said normal cells.

30. (new) The method according to claim 29, wherein the pre-treatment is carried out for a time greater than or equal to the cell cycle duration of said proliferating normal cell.

31. (new) The method according to claim 28, wherein, after the combined treatment, a post treatment is carried out including interrupting the administration of said class B compound and washing said class B compound off the culture while maintaining the administration of said class A compound.

32. (new) The method according to claim 31, wherein the combined treatment is carried out for a time greater than or equal to the cell cycle duration of said tumor cells having an inactivated p53 pathway.

33. (new) The method according to claim 31, wherein said washing step is carried out for a time greater than or equal to 3 hours.

34. (new) The method according to claim 30 or 31, wherein said combined treatment, pre-treatment and/or post-treatment is repeated twice or more.

35. (new) The method according to claim 28, wherein the chemotherapeutic compound (class B compound) is selected from the group consisting of folate inhibitors, nucleoside analogues, nucleotide synthesis inhibitors, vinca alkaloids, taxanes, colchicine derivatives, podophillotoxin derivatives, and topoisomerase inhibitors and the protective compound (class A compound) is selected from the group consisting of cytochalasins, jasplakinolides, chondramides, isoindolinones, and latrunculines, with the exclusion of cytochalasin B.

36. (new) The method according to claim 35, wherein said protective compound is selected from the group consisting of the cytochalasin D, dihydrocytochalasin B, jasplakinolide, chondramide B and latrunculin B.

37. (new) The method according to claim 35, wherein said chemotherapeutic compound is selected from the group consisting of trifluorothymidine, cytarabine, 6-thioguanine, 6-mercaptoputrine, gemcytabine, fludarabine, floxuridine, ftorafur, methotrexate, trimetrexate, raltitrexed, edatrexate, lometrexol, hydroxyurea, vincristine, vinblastine, vinorelbin, vindesine, paclitaxel, docetaxel, irinotecan, topotecan, 9-amino-S(20)-camptothecine.

38. (new) The method according to claims 28, wherein C3H10T1/2 cells or cells derived therefrom are used as model cells.

39. (new) The method according to claim 38, wherein C3H10T1/2 cells or cells derived therefrom are used as model cells for identifying a protective compound and/or a chemotherapeutic compound.

40. (new) A method for protecting proliferating normal cells in an *in vivo* treatment of tumor cells having an inactive p53 pathway, from the eradication of a chemotherapeutic compound (class B compound),

said method comprising administering to said culture the chemotherapeutic compound in combination with a protective compound (class A compound),

the chemotherapeutic compound having the capability of

- exerting a cytotoxic action toward actively proliferating cells,
  - not affecting survival and proliferative potential of interphase cells,
- the protective compound having the capability of
- reversibly inhibiting cytodieresis of normal cells,
  - not inhibiting the biological action of said chemotherapeutic compound and,

wherein a pre-treatment with said protective compound is carried out before the combined treatment with class A and class B compounds and the administration of said protective compound results in the protection of at least part of said proliferating normal cells.

41. (new) The method according to claim 40, wherein the pre-treatment with the protective compound results in the arrest at interphase of at least part of said normal cells.

42. (new) The method according to claim 41, wherein the pre-treatment is carried out for a time greater than or equal to the cell cycle duration of said proliferating normal

cell.

43. (new) The method according to claim 40, wherein, after the combined treatment, a post treatment is carried out including interrupting the administration of said class B compound and washing said class B compound off the subject tissues while maintaining the administration of said class A compound.

44. (new) The method according to claim 43, wherein the combined treatment is carried out for a time greater than or equal to the cell cycle duration of said tumor cells having an inactivated p53 pathway.

45. (new) The method according to claim 43, wherein said washing step is carried out for a time greater than or equal to 3 hours.

46. (new) The method according to claim 42 or 43, wherein said combined treatment, pre-treatment and/or post-treatment is repeated twice or more.

47. (new) The method according to claim 40, wherein the chemotherapeutic compound (class B compound) is selected from the group consisting of folate inhibitors, nucleoside analogues, nucleotide synthesis inhibitors, vinca alkaloids, taxanes, colchicine derivatives, podophyllotoxin derivatives, and topoisomerase inhibitors and the protective compound (class A compound) is selected from the group consisting of cytochalasins, jasplakinolides, chondramides, isoindolinones, and latrunculines, with the exclusion of cytochalasin B.

48. (new) The method according to claim 47, wherein said protective compound is selected from the group consisting of the cytochalasin D, dihydrocytochalasin B, jasplakinolide, chondramide B and latrunculin B.

49. (new) The method according to claim 47, wherein said chemotherapeutic compound is selected from the group consisting of trifluorothymidine, cytarabine, 6-thioguanine, 6-mercaptopurine, gemcytabine, fludarabine, floxuridine, ftorafur, methotrexate, trimetrexate, raltitrexed, edatrexate, lometrexol, hydroxyurea, vincristine, vinblastine, vinorelbin, vindesine, paclitaxel, docetaxel, irinotecan, topotecan, 9-amino-S(20)-camptothecine.

50. (new) The method according to claim 40, wherein the tumor is a tumor form having a low proliferating potential.

51. (new) The method according to claim 40, wherein the tumor form is an hyperproliferative lesion cause by papilloma virus.

52. (new) A method for protecting normal cells in an *in vivo* treatment of a pathological infection caused by microorganisms displaying no p53 function, from the eradivative action of a chemotherapeutic compound (class B compound),

said method comprising administering to said culture the chemotherapeutic compound in combination with a protective compound (class A compound),

the chemotherapeutic compound having the capability of

- exerting a cytotoxic action toward actively proliferating cells,
- not affecting survival and proliferative potential of interphase cells,

the protective compound having the capability of

- reversibly inhibiting cytodieresis of normal cells,
- not inhibiting the biological action of said chemotherapeutic compound and,

wherein the administration of said protective compound results in the protection of at

least part of said normal cells.

53. (new) A method for preventing and treating halopecia associated to a systemic treatment with a chemotherapeutic compound, said method comprising administering the chemotherapeutic compound in combination with a protective compound, the chemotherapeutic compound having the capability of

- exerting a cytotoxic action toward actively proliferating cells,
  - not affecting survival and proliferative potential of interphase cells,
- the protective compound having the capability of
- reversibly inhibiting cytodieresis of normal cells,
  - not inhibiting the biological action of said chemotherapeutic compound.

54. (new) The method according to claims 52 or 53 wherein the chemotherapeutic compound is selected from the group consisting of folate inhibitors, nucleoside analogues, nucleotide synthesis inhibitors, vinca alkaloids, taxanes, colchicine derivatives, podophillotoxin derivatives, and topoisomerase inhibitors and the protective compound is selected from the group consisting of cytochalasins, jasplakinolides, chondramides, isoindolinones, and latrunculines, with the exclusion of cytochalasin B.

55. (new) The method according to claim 54, wherein said protective compound is selected from the group consisting of the cytochalasin D, dihydrocytochalasin B, jasplakinolide, chondramide B and latrunculin B.

56. (new) The method according to claim 54, wherein said chemotherapeutic compound is selected from the group consisting of trifluorothymidine, cytarabine, 6-thioguanine, 6-mercaptoputrine, gemcytabine, fludarabine, floxuridine, ftorafur,

methotrexate, trimetrexate, raltitrexed, edatrexate, lometrexol, hydroxyurea, vincristine, vinblastine, vinorelbin, vindesine, paclitaxel, docetaxel, irinotecan, topotecan, 9-amino-S(20)-camptothecine.

57. (new) The method according to claims 52 or 53 wherein a pre-treatment with said protective compound is carried out before the combined treatment with class A and class B compounds.

58. (new) A pharmaceutical composition for selectively eradicating cells having inactive p53 pathway comprising therapeutically effective amounts of a protective compound, a chemotherapeutic compound and a pharmaceutically acceptable vehicle, carrier or auxiliary agent, the chemotherapeutic compound having the capability of

- exerting a cytotoxic action toward actively proliferating cells,
  - not affecting survival and proliferative potential of interphase cells,
- the protective compound having the capability of
- reversibly inhibiting cytodieresis of normal cells,
  - not inhibiting the biological action of said chemotherapeutic compound, wherein the release of the chemotherapeutic compound is retarded with respect to the release of the protective compound.

59. (new) Pharmaceutical composition according to claim 58, wherein the chemotherapeutic compound is selected from the group consisting of folate inhibitors, nucleoside analogues, nucleotide synthesis inhibitors, vinca alkaloids, taxanes, colchicine derivatives, podophyllotoxin derivatives, and topoisomerase inhibitors and the protective compound is selected from the group consisting of cytochalasins, jasplakinolides,

chondramides, isoindolinones, and latrunculines, with the exclusion of cytochalasin B.

60. (new) A pharmaceutical composition according to claim 59 wherein said protective compound is selected from the group consisting of the cytochalasin D, dihydrocytochalasin B, jasplakinolide, chondramide B and latrunculin B,

61. (new) A pharmaceutical composition according to claim 59, wherein said chemotherapeutic compound is selected from the group consisting of trifluorothymidine, cytarabine, 6-thioguanine, 6-mercaptoputrine, gemcytabine, fludarabine, floxuridine, ftorafur, methotrexate, trimetrexate, raltitrexed, edatrexate, lometrexol, hydroxyurea, vincristine, vinblastine, vinorelbin, vindesine, paclitaxel, docetaxel, irinotecan, topotecan, 9-amino-S(20)-camptothecine.

62. (new) Pharmaceutical composition according to 58 in the treatment of a tumor form having an inactive p53 pathway or in the treatment of pathological infection associated to a microorganism having no p53 function or in the treatment of hyperproliferative lesions caused by papillomavirus infection.

63. (new) A kit of parts for selectively eradicating cells having an inactive p53 pathway and selectively protecting proliferating normal cells comprising a protective compound and a chemotherapeutic compound, the chemotherapeutic compound having the capability of

- exerting a cytotoxic action toward actively proliferating cells,
  - not affecting survival and proliferative potential of interphase cells,
- the protective compound having the capability of
- reversibly inhibiting cytodieresis of normal cells,



- not inhibiting the biological action of said chemotherapeutic compound, the kit being for the sequential administration of the protective compound alone firstly, and then of the association of the protective and chemotherapeutic compounds.

64. (new) Kit of parts according to claim 63 in the treatment of a tumor form having an inactive p53 pathway or in the treatment of pathological infection associated to a microorganism having no p53 function or in the treatment of hyperproliferative lesions caused by papillomavirus infection.

65. (new) Kit of parts according to claim 63 wherein the chemotherapeutic compound is selected from the group consisting of folate inhibitors, nucleoside analogues, nucleotide synthesis inhibitors, vinca alkaloids, taxanes, colchicine derivatives, podophillotoxin derivatives, and topoisomerase inhibitors and the protective compound is selected from the group consisting of cytochalasins, jasplakinolides, chondramides, isoindolinones, and latrunculines, with the exclusion of cytochalasin B.

66. (new) Kit of parts according to claim 65 wherein said protective compound is selected from the group consisting of the cytochalasin D, dihydrocytochalasin B, jasplakinolide, chondramide B and latrunculin B.

67. (new) Kit of parts according to claim 65, wherein said chemotherapeutic compound is selected from the group consisting of trifluorothymidine, cytarabine, 6-thioguanine, 6-mercaptoputrine, gemcytabine, fludarabine, floxuridine, ftorafur, methotrexate, trimetrexate, raltitrexed, edatrexate, lometrexol, hydroxyurea, vincristine, vinblastine, vinorelbin, vindesine, paclitaxel, docetaxel, irinotecan, topotecan, 9-amino-S(20)-camptothecine.

68. (new) Method of using of a protective compound having the capability of

- reversibly inhibiting cytodieresis of normal cells,
- not inhibiting the biological action of a chemotherapeutic compound, which chemotherapeutic compound has the capability of
  - exerting a cytotoxic action toward actively proliferating cells, but
  - not affecting survival and proliferative potential of interphase cells,

for the preparation of the pharmaceutical composition according to claim 58 or the kit according to claim 63.

69. (new) Method according to claim 68 wherein the protective compound is selected from the group consisting of cytochalasins, jasplakinolides, chondramides, isoindolinones, and latrunculines, with the exclusion of cytochalasin B

70. (new) Method according to claim 69, wherein the protective compound is selected from the group consisting of the cytochalasin D, dihydrocytochalasin B, jasplakinolide, chondramide B and latrunculin B.--